UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,891	07/17/2003	Graham Alan March	GAM 6410.1	2751

321 7590 12/19/2007

SENNIGER POWERS
ONE METROPOLITAN SQUARE
16TH FLOOR
ST LOUIS, MO 63102

EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
12/19/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

Office Action Summary	Application No.	Applicant(s)	
	10/622,891	MARCH, GRAHAM ALAN	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-15,18-26,29-32 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-3, 6-15, 18-26, 29-32,63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 10/05/2007, wherein claims 1, 10, 11, 13, 19, 20, 22, 23, and 31 have been amended, and claims 4-5, 16-17, and 27-28 have been cancelled. Applicant's amendment also added new claim 63.

Applicant arguments with respect to the recitation "aromatic flavoring agent" in the claims have been considered, and found persuasive. The rejection of claims 1, and 6 under 35 U.S.C. 112, second paragraph, as being indefinite is herein withdrawn.

Applicant arguments with respect to the recitation "effective amounts being selected so as to mask substantially the bitter taste and pungent odor of sodium 4-phenylbutyrate" in claims 10, 20-22 and "the effective amounts being selected so as to mask substantially the bitter taste following dilution" in claim 13 have been considered, and found persuasive. The rejection of claims 10, 13-17, 20-22 under 35 U.S.C. 112, second paragraph, as being indefinite is herein withdrawn.

Claims 1-3, 6-15, 18-26, 29-32, and 63 are examined herein on the merits as they read on the elected invention.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1) Claims 13-15, 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "up to the solubility limit thereof measured at 10 °C" in claim 13 is vague. It is not clear what the applicant means by this recitation.

2) Claims 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "binding amount of a binding agent" in claim 23 render the claims vague, and indefinite. The recitation "binding amount of a binding agent" is not defined in claim, and the specification does not provide information as to how much is the binding amount of a binding agent that can be used in the instant composition.

3) Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recites the limitation "artificial water soluble sweetening agent" in the claim. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 6, 10, and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Samid et al. (6,037,376, PTO-892), in view of Rubenstain et al. (US 2002/0115619, PTO-892), and further in view of Blase et al. (US 5,272,137, PTO-892).

Samid et al. discloses pharmaceutical compositions comprising sodium phenylbutyrate, a water soluble sweetening agent, sugar, and a binder, Sterotex. See column 25-26, EXAMPLE 18, EXAMPLE 21, and EXAMPLE 21.

Samid et al. do not explicitly teach an aromatic flavoring agent.

Samid et al. do not teach the employment of the particular synthetic sweetening agents aspartame and potassium acesulfame.

Rubenstain et al. (US 2002/0115619, PTO-892) teach that sodium 4-phenylbutyrate has bad taste in the mouth. See page 13, paragraph [0143]. Rubenstain et al. teaches that compositions in the form of Tablet therein can contain sweetening agent, a flavoring agent, or some combinations thereof in order to provide pharmaceutically elegant and palatable preparation. See page 8, paragraphs [0097]-[0105]; paragraph [0112].

Blase et al. teaches taste masked pharmaceutical compositions. It is taught that artificial sweeteners, and fruit flavoring agents are employed in the pharmaceutical compositions to mask the disagreeable taste of the pharmaceutically active agent. See abstract; column 1, lines 6-10; 62-68; column 4, lines 29-34, line 55-column 4, line 6, column 5. It is disclosed that artificial sweeteners such as aspartame, acesulfame

potassium, saccharin, sucrolose or mixtures, and fruit flavors such as cherry, grape, orange, strawberry or lemon are employed. It is also taught that the amount of artificial sweetener used in the pharmaceutical composition therein can be upto 5 grams per 100 mL of suspension. The flavoring agent can be present in an amount upto 5 grams per 100 mL of the suspension. See line 55-column 4, line 6, column 5; column 10, claims 1, 4.

It would have been obvious to a person of ordinary skill in the art at the time of invention to employ aromatic flavoring agents, and specific synthetic sweetening agents aspartame and potassium acesulfame in the compositions comprising sodium 4-phenylbutyrate taught by Samid et al. because 1) Rubenstain et al. teach that sodium 4-phenylbutyrate has a bad taste, and also teaches that the compositions comprising sodium 4-phenylbutyrate can contain flavoring agents, and artificial sweetening agents, and 2) Blasé et al. teach that aspartame, acesulfame potassium, saccharin, sucrolose or mixtures, and fruit flavors such as cherry, grape, orange, strawberry or lemon are employed in pharmaceutical compositions to mask the disagreeable taste of the pharmaceutically active agent. Thus, one of ordinary skill in the art at the time of invention would have been motivated to employ the well known fruit flavoring agent, strawberry flavoring agent, and the well artificial sweeteners with reasonable expectation of obtaining a pharmaceutical composition that is palatable, and masks the disagreeable taste of sodium 4-phenylbutyrate.

Furthermore, as the combined teachings of Samid et al., Rubenstein et al., Blase et al. renders the claimed pharmaceutical composition obvious, the property of such a

claimed composition will also be rendered obvious by the prior art teachings, since the properties, namely to mask substantially the bitter taste and pungent odor of sodium 4-phenylbutyrate in independent claim 10 are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art product does not possess or render obvious the same properties as the instantly claimed product.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 6-15, 18-26, 29-32, and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubenstain et al. (US 2002/0115619, PTO-892), in view of Blase et al. (US 5,272,137, PTO-892).

Rubenstein et al. discloses a pharmaceutical composition comprising sodium 4-phenylbutyrate. See page 2, paragraph [0019], [0022]; page 11, [0122]; page 13, [0143]. It is also taught that the pharmaceutical compositions therein can be in the form of a tablet, a soft capsule, a chachet, a troche, or a lozenge. The formulations for oral

administration include, a powdered or granular formulation, an aqueous or oily suspension, an aqueous or oily solution or emulsion. The compositions therein can contain binding agents such as polyvinylpyrrolidone, hydroxypropyl methylcellulose. The compositions comprise from 0.1 % to 100 % (w/w) active ingredient. Page 8, paragraph [0094]. It is also disclosed that sodium 4-phenylbutyrate has bad taste in the mouth. See page 13, paragraph [0143]. The compositions in the form of Tablet therein can contain sweetening agent, a flavoring agent, or some combinations thereof in order to provide pharmaceutically elegant and palatable preparation. Sweetening agents include glycerol, propylene glycol, sorbitol, sucrose, and saccharin i.e a synthetic sweetening agent. See page 8, paragraphs [0097]-[0105]; paragraph [0112]. It is also taught that the pharmaceutical compositions therein can be in a single or multi unit-dose. See page 8, paragraph [0090].

Rubenstein et al. do not explicitly teach an aromatic flavoring agent.

Rubenstein et al. do not teach the employment of the particular synthetic sweetening agents aspartame and potassium acesulfame.

Rubenstein does not specifically teach the particular amounts of flavoring agents, sweetening agents, and binding agent in the composition therein.

Blase et al. teaches taste masked pharmaceutical compositions. It is taught that artificial sweeteners, and fruit flavoring agents are employed in the pharmaceutical compositions to mask the disagreeable taste of the pharmaceutically active agent. See abstract; column 1, lines 6-10; 62-68; column 4, lines 29-34, line 55-column 4, line 6, column 5. It is disclosed that artificial sweeteners such as aspartame, acesulfame

potassium, saccharin, sucrolose or mixtures, and fruit flavors such as cherry, grape, orange, strawberry or lemon are employed. It is also taught that the amount of artificial sweetener used in the composition therein can be upto 5 grams per 100 mL of suspension. The amount of flavoring agent can be present in an amount upto 5 grams per 100 mL of the suspension. See line 55-column 4, line 6, column 5; column 10, claims 1, 4.

It would have been obvious to a person of ordinary skill in the art at the time of invention to employ aromatic flavoring agents, and specific synthetic sweetening agents aspartame and potassium acesulfame in the compositions comprising sodium 4-phenylbutyrate because 1) Rubenstein et al. teach that sodium 4-phenylbutyrate has a bad taste, and also teaches that the compositions comprising sodium 4-phenylbutyrate can contain flavoring agents, and artificial sweetening agents, and 2) Blase et al. teach that aspartame, acesulfame potassium, saccharin, sucrolose or mixtures in amount upto 5 grams per 100 mL of composition, and fruit flavors such as cherry, grape, orange, strawberry or lemon in an amount upto 5 grams per 100 mL of the composition are employed in pharmaceutical compositions to mask the disagreeable taste of the pharmaceutically active agent . Thus, one of ordinary skill in the art at the time of invention would have been motivated to employ the well known fruit flavoring agent, strawberry flavoring agent, and the well artificial sweeteners with reasonable expectation of obtaining a pharmaceutical composition that is palatable, and masks the disagreeable taste of sodium 4-phenylbutyrate.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as amounts of flavoring agents, sweetening agents, and binding agent employed in the composition of Rubenstein et al., to obtain a pharmaceutical composition.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the amounts of flavoring agents, sweetening agents, and binding agent employed in the compositions, since Blase et al. teach such amounts of flavoring agents, sweetening agents, and further the optimization of amounts of known agents in a composition, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Furthermore, as the combined teachings of Rubenstein et al., Blase et al. renders the claimed pharmaceutical composition obvious, the property of such a claimed composition will also be rendered obvious by the prior art teachings, since the properties, namely to mask substantially the bitter taste and pungent odor of sodium 4-phenylbutyrate in independent claims 10, 13, 20, 22 are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See

MPEP 2112.01. The burden is shifted to Applicant to show that the prior art product does not possess or render obvious the same properties as the instantly claimed product.

It is pointed out that the recitation "the unit dose prepared by diluting with water an aliquot of a concentrated aqueous solution containing at atleast about 200 mg/ml of up the solubility limit thereof measured at 10 °C" in instant claim 20, and "wherein the granules are mixed with the at least one synthetic water soluble softening agent and with at least one water soluble flavoring agent to form the wetted mass" in claim 31, are product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 ('Fed. Cir. 1985). See MPEP 21 13.

Response to Arguments

Applicant's remarks that "most of the children rejected treatment with phenylbutyrate because of the taste and could not be treated. The clinical trial was for the use of sodium phenylbutyrate to treat sickle cell anaemia. This is an, as yet, unproven treatment." These remarks have been considered. It is pointed out that the instant claims are drawn to composition comprising sodium 4-phenylbutyrate, and not to the method of treatment. As the combined teachings of Samid et al., Rubenstein et

al., Blase et al. renders the claimed pharmaceutical composition obvious, the property of such a claimed composition will also be rendered obvious by the prior art teachings, since the properties, namely to mask substantially the bitter taste and pungent odor of sodium 4-phenylbutyrate in independent claim 10 are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art product does not possess or render obvious the same properties as the instantly claimed product.

Applicant argues that "the enclosed journal article makes it clear that the general understanding of the industry was that the problems associated with phenylbutyrate were so great that they were unlikely to be solved without THE INGENUITY of the pharmaceutical manufacturers. It is this ingenuity that the applicants have now shown." These arguments have been considered, but not found persuasive. Rubenstain et al. teach that the compositions containing phenylbutyrate in the form of Tablet therein can contain sweetening agent, a flavoring agent, or some combinations thereof in order to provide pharmaceutically elegant and palatable preparation. Blase et al. teaches taste masked pharmaceutical compositions. It is taught that artificial sweeteners, and fruit flavoring agents are employed in the pharmaceutical compositions to mask the disagreeable taste of the pharmaceutically active agent. It would have been obvious to a person of ordinary skill in the art at the time of invention to employ aromatic flavoring agents, and specific synthetic sweetening agents aspartame and potassium acesulfame

in the compositions comprising sodium 4-phenylbutyrate because 1) Rubenstein et al. teach that sodium 4-phenylbutyrate has a bad taste, and also teaches that the compositions comprising sodium 4-phenylbutyrate can contain flavoring agents, and artificial sweetening agents, and 2) Blase et al. teach that aspartame, acesulfame potassium, saccharin, sucrolose or mixtures in amount upto 5 grams per 100 mL of composition, and fruit flavors such as cherry, grape, orange, strawberry or lemon in an amount upto 5 grams per 100 mL of the composition are employed in pharmaceutical compositions to mask the disagreeable taste of the pharmaceutically active agent . Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to employ the well known fruit flavoring agent, strawberry flavoring agent, and the well known artificial sweeteners with reasonable expectation of obtaining a pharmaceutical composition that is palatable, and masks the disagreeable taste of sodium 4-phenylbutyrate.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Tuesday-Thursday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit : 1617

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER